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Use of sensor-integrated pump therapy to reduce hypoglycaemia in people with Type 1 diabetes: a real-world study in the UK

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What's new?

- Insulin pumps that automatically suspend insulin delivery based on actual or predicted low glucose levels reduce nocturnal and overall hypoglycaemia in randomized controlled trials, but even with these devices some people continue to struggle with nocturnal hypoglycaemia.
- This is one of the first real-world studies to assess the effectiveness of automated insulin suspension systems.
- Both daytime and nocturnal hypoglycaemia were reduced to low levels.
- Automated insulin suspension in response to hypoglycaemia can reduce the burden of hypoglycaemia in real-world clinical practice.
- These reductions in hypoglycaemia are achieved with no loss of mean glucose control.
- Predictive suspension of insulin adds incremental value to threshold suspend systems.

Abstract

Aims To assess the efficacy of insulin pumps with automated insulin suspension systems in a real-world setting.

Methods We analysed anonymized data uploaded to CareLink™ by people ($n=920$) with Type 1 diabetes using the MiniMed Paradigm Veo system and the MiniMed 640G system (Medtronic International Trading Sàrl, Tolochanez, Switzerland) with SmartGuard technology, with or without automated insulin suspension enabled, between February 2016 and June 2018. Users with ≥ 15 days of sensor data and $\geq 70\%$ sensor-wear time were classified as sensor-augmented pump alone, sensor-integrated pump with low glucose suspend enabled or sensor-integrated pump with predictive low glucose management enabled.

Results The median (25th–75th percentile) system use was 161 (58–348) days. The median time spent with sensor glucose values ≤ 3 mmol/l was 0.8 (0.3–1.7)% in the sensor-augmented pump group, 0.3 (0.1–0.7)% in the sensor-integrated pump with low glucose suspend group, and 0.3 (0.1–0.5)% in the sensor-integrated pump with predictive low glucose management group. In individuals switching from sensor-augmented pump to sensor-integrated pump with low glucose suspend ($n=31$), there were

significant reductions in the monthly rate of hypoglycaemic events <3 mmol/l (rate ratio 0.63, 95% CI 0.45–0.89; $P=0.009$) and in the percentage of time with glucose values ≤ 3 mmol/l [sensor-augmented pump: 0.63% (95% CI 0.34–1.29), sensor-integrated pump with low glucose suspend: 0.33% (95% CI 0.16–0.64); $P=0.001$]. The monthly rate of hypoglycaemic events decreased further in individuals ($n=139$) switching from sensor-integrated pump with low glucose suspend to sensor-integrated pump with predictive low glucose management [rate ratio 0.82 (95% CI 0.69–0.98); $P<0.0274$]. Similar results were seen for events <3.9 mmol/l. There was no difference in median time spent in target glucose range.

Conclusion Real-world UK data show that increasing automation of insulin suspension reduces hypoglycaemia exposure in people with Type 1 diabetes.

Introduction

The importance of tight glycaemic control to reduce the vascular complications of Type 1 diabetes mellitus is well established [1], but hypoglycaemia can present a significant barrier to achieving such control [2,3]. In recent years, the management of Type 1 diabetes has been transformed by continuous glucose monitoring (CGM), which can be used with or without insulin pump therapy. Although CGM alone can potentially improve glycaemic control and reduce hypoglycaemia [4,5], sensor-integrated pump therapy, which combines continuous subcutaneous insulin infusion (CSII) with real-time CGM, offers the opportunity for automated insulin suspension to prevent or minimize the risk of harm resulting from hypoglycaemia. This approach has been shown to provide improved glycaemic control compared with CSII or multiple daily injections with self-monitoring of blood glucose, but its effects on the rate of severe hypoglycaemia have been less consistent [6–9].

With sensor-augmented pump (SAP) therapy, the user can read the CGM data at any time or can be alerted to pre-set levels of high or low glucose readings by alerts, and then has to decide the appropriate action in response to these values [10]. In recent years, the technology has evolved to

incorporate features such as 'low glucose suspend', or 'suspend before low', with the latter hereafter referred to as predictive low glucose management, which are intended to minimize the risk of hypoglycaemia without user intervention. With the low glucose suspend feature, insulin delivery is temporarily suspended if glucose levels drop below a predefined threshold level. Delivery automatically resumes after 2 h, unless the user manually overrides the suspension within this time. Predictive low glucose management is a more sophisticated technology, whereby insulin delivery can be suspended according to predicted hypoglycaemia within the next 30 min, and delivery is automatically resumed once blood glucose levels start to recover. Such technologies, in which the pump automatically suspends insulin delivery according to actual or predicted low glucose levels, have been referred to as sensor-integrated pump therapies [10]. Clinical studies have shown that sensor-integrated pump therapy reduces the risk of severe or nocturnal hypoglycaemia, compared with pump therapy without low glucose suspend [2], and this has been confirmed in a recent systematic review [11]. Based on these studies, in 2015, the UK National Institute for Health and Care Excellence (NICE) recommended the MiniMed® Paradigm™ Veo™ system (Medtronic International Trading Sàrl, Tolochanez, Switzerland) as an option for the management of blood glucose levels in people with Type 1 diabetes who have episodes of disabling hypoglycaemia despite optimal management with CSII therapy [12]. Subsequently, the MiniMed Paradigm Veo system was superseded by the Medtronic MiniMed 640G system with SmartGuard™ technology, and the company was asked by NICE to publish real-world data in the UK setting for these systems.

As with all new technology, it is becoming increasingly important to demonstrate the generalizability of the improvements in glycaemic control and rates of hypoglycaemia seen in controlled clinical trials to the real-world situation [13]. Individuals with recurrent severe hypoglycaemia are likely to be those offered these systems in the UK, but were excluded from published studies such as ASPIRE, and there are data showing that hypoglycaemia rates are higher in real-world settings than in clinical trials [14]. Hence, a retrospective analysis of CareLink™ data from people with Type 1 diabetes in the UK was conducted to determine the real-world effectiveness of sensor-integrated pump therapy with the MiniMed Paradigm Veo or MiniMed 640G systems.

Participants and methods

CareLink Personal is a web-based therapy management software package, which provides remote storage of, and access to, insulin pump and CGM data. The system has remote storage and retrospective analysis capabilities and can be used to access and analyse real-world treatment outcomes in people with diabetes. The CareLink database includes only participants receiving insulin pumps or sensor-integrated pump treatment from Medtronic, and blood glucose meters from various manufacturers. It is password-protected, and compliant with data privacy protection laws. When participants sign up to a CareLink account they have the option to provide consent for their data to be used for research purposes. On registration, individuals self-report age group, gender and type of diabetes, but other demographic data are not included in CareLink.

Participant population

The present analysis included data from individuals with self-reported Type 1 diabetes in the UK who had signed up to a Carelink account and given consent for their anonymized data to be used for research. Self-reported age category and sex data are captured from CareLink software. To be eligible for inclusion, participants were required to have had at least 15 days of sensor data within the 2-year observation period from 12 February 2016 (when the NICE recommendations [16] were issued) to 12 June 2018, and to have used the sensor for at least 70% of the time during their sensor usage period.

Participants were categorized according to the suspension mode used. Individuals not using any insulin suspension mode were categorized as SAP, those using pump therapy with low glucose suspend feature enabled as LGS, and those using pump therapy with predictive low glucose management enabled as PLGM.

For each participant, and each suspension mode, the following measures were calculated: duration of use (days); mean sensor glucose values; time with sensor glucose values ≤ 3.0 mmol/l, ≤ 3.9 mmol/l and between >3.9 and <10 mmol/l; overall, daytime and nocturnal number of excursions per month <3 mmol/l and <3.9 mmol/l; and estimated HbA_{1c} (mmol/mol).

A hypoglycaemic event was defined as a sensor glucose level <3.0 mmol/l or <3.9 mmol/l, which was maintained for at least 20 min, with a gap of at least 20 min between events [15]; more than one low blood glucose measurement occurring within 20 min was regarded as a single event. This analysis used a 20-min duration as a criterion for a hypoglycaemic event because this includes at least three separate measurements when CGM measures glucose every 5 min. Daytime hypoglycaemic events were defined as occurring between 8:00 h and 24:00 h.

Estimated HbA_{1c} was calculated from mean sensor glucose, as described by Nathan *et al.* [16].

Statistical analysis

Because of limitations in the CareLink dataset and data privacy protection law, specific clinical information and baseline data are not available. Hence, no valid direct between-group comparisons could be performed as we could not adjust the analysis to avoid possible bias, and so only descriptive statistics are reported for participants aged ≤ 15 years (children) and those aged >15 years (defined in the present study as adults) for instances of use in predefined groups, based on the suspension mode used: SAP, LGS, and PLGM. For each participant, the average sensor glucose value was calculated using sensor glucose readings during the time the participant was using a specific suspension mode: none (SAP alone), LGS or PLGM. The median and other summary statistics of sensor glucose values in the suspension mode were calculated using these participant-averaged glucose values.

Valid between-group comparisons of glycaemic variables were possible for individuals who changed between SAP, LGS or PLGM during the study period. These paired comparisons were performed using Wilcoxon signed rank tests, because the normality assumption of the data was not met according to the Shapiro–Wilk test. A negative binomial generalized linear mixed model with a log link was used to compare the rates of sensor hypoglycaemic events with different suspension modes. As participants provided data both for different suspension modes, and for the same suspension mode at different times during the study period, correlated data were accounted for by using participant as a random intercept in the mixed model.

All statistical analyses were performed using SAS (version 9.4) software (SAS Institute, Cary, NC, USA), and *P* values <0.05 were taken to indicate statistical significance.

Results

Of 9755 individuals in the UK with Type 1 diabetes registered with CareLink, 9192 (94.2%) gave consent for their data to be used for research, of whom 1634 individuals using insulin pumps and glucose sensors uploaded data to the CareLink database over the 2-year observation period. Of these, 920 (56.3%) met the inclusion criteria of at least 70% sensor use and at least 15 days using the technology; 798 (86.7%) used MiniMed 640G pumps, 65 (7.1%) used Veo pumps and 57 (6.2%) used both. Overall, 401 (43.6%) were adults (aged >15 years).

In total, 96 participants used SAP therapy alone (i.e. no suspend feature enabled in 28 instances with Veo and 75 instances with 640G), 249 used LGS (low glucose suspend feature enabled in 104 instances with Veo and 158 instances with 640G), and 781 used PLGM (all with 640G). In the overall study population (*n*=920) the total number of days with sensor in the observation period was 250 432, and the median (25th–75th percentile) sensor usage rate per participant was 98 (90–100)%.

Descriptive analyses of glycaemic measures and use of glucose suspend features for both children and adults are summarized in Table 1. In adults, the median (25th–75th percentile) percentage of time with sensor glucose value ≤ 3 mmol/l was 0.9 (0.3–2.1)% with SAP alone, 0.3 (0.1–0.7)% with LGS, and 0.2 (0.1–0.5)% with PLGM, while in children the median (25th–75th percentile) percentage of time spent with sensor glucose values ≤ 3 mmol/l was 0.8 (0.4–1.5)%, 0.3 (0.2–0.7)% and 0.3 (0.1–0.5)%, in the respective groups. In general, suspension feature usage and glycaemic profiles were similar in adults and children; the median number of suspensions was numerically higher in children than in adults, but the median duration of suspension was shorter (Table 1).

Within-participant comparison of therapies

During the observation period, a total of 187 participants switched from one suspension mode to another, allowing within-participant comparisons of different technologies. Comparisons of SAP vs LGS were made in 31 participants, SAP vs PLGM in 55 participants, and LGS vs PLGM in 139 participants. . The duration of usage, time below hypoglycaemic thresholds, monthly rate of hypoglycaemic excursions and time in range in the SAP to LGS, SAP to PLGM and LGS to PLGM groups are summarised in Table 2. The median duration of use was significantly ($P<0.0001$) longer with PLGM compared with either SAP with no suspension on or LGS, but there was no significant difference between the duration of SAP or LGS use in the SAP to LGS group.

SAP vs LGS

In participants who switched from SAP to LGM ($n=31$), the monthly rate of sensor hypoglycaemic events <3 mmol/l decreased by 37% (model-based event rate ratio 0.63, 95% CI 0.45– 0.89; $P=0.009$), and the median (25th–75th percentile) percentage of time spent with glucose values ≤ 3 mmol/l was also reduced: SAP 0.63 (0.34–1.29)%; LGS 0.33 (0.16–0.64); $P=0.001$). Similarly, the monthly rate of sensor hypoglycaemic events <3.9 mmol/l was reduced by 19% following the switch from SAP to LGS: event rate ratio 0.81 (95% CI 0.67, 0.98); $P=0.033$, and the percentage of time with sensor glucose ≤ 3.9 mmol/l decreased from 4.0 (2.6–5.3)% to 2.6 (0.19–0.41)% ($P=0.0028$).

The median (25th–75th percentile) time per day with blood glucose ≤ 3 mmol/l was significantly lower in the LGS period, compared with the SAP period (5.0 [2–9] min vs 9.0 [5–9] min, respectively; $P=0.001$), as were the corresponding times with sensor glucose ≤ 3.9 mmol/l (38.0 [27–58] min vs 57 [37–76] min, respectively; $P=0.0028$). Thus, LGS was associated with 44% less time spent with glucose ≤ 30 mmol/l, and 33% less time ≤ 3.9 mmol/l, compared with SAP.

SAP vs PLGM

In participants who switched from SAP to PLGM ($n=55$), the monthly rate of sensor hypoglycaemic events decreased by 49% (event rate ratio 0.51, 95% CI 0.38, 0.69; $P<0.0001$), and the percentage of time ≤ 3 mmol/l was reduced from 0.8 (0.4–1.6)% with SAP to 0.3 (0.1;0.6)% with PLGM ($P=0.001$). The corresponding monthly rate of hypoglycaemic events <3.9 mmol/l was reduced by 32% [event rate ratio 0.68 (95% CI 0.58–0.80); $P<0.0001$], and the percentage of time below this level decreased from 4.3 (2.1–6.3)% with SAP alone to 2.3 (1.4–3.5) with PLGM ($P=0.001$).

LGS vs PLGM

A total of 139 participants switched from LGS to PLGM. In these participants, the monthly rate of sensor hypoglycaemic events <3.0 mmol/l decreased by 18% during the PLGM period, compared with the LGS period [event rate ratio 0.82 (95% CI 0.69, 0.98); $P<0.0274$], and the percentage of time with glucose values ≤ 3 mmol/l also decreased, albeit not significantly: LGS 0.3 (0.1, 0.5)%; PLGM 0.4 (0.1–0.7)%; $P=0.091$. Similarly, the monthly rate of sensor hypoglycaemic events <3.9 mmol/l decreased by 21%, compared with the LGS period [event rate ratio 0.79 (95% CI 0.7, 0.88); $P<0.0001$], and the median (25th–75th percentile) percentage of time with glucose values ≤ 3.9 mmol/l was also significantly lower during the PLGM period: LGS 1.8 (0.8–3.0)%; PLGM 2.1 (1.2–3.9)%; $P<0.0001$.

The median (25th–75th percentile) duration per day with sensor glucose values ≤ 3 mmol/l was 5.0 (2–10) min in the LGS group and 4.0 (1–8) min in the PLGM group ($P=0.009$); the median times with sensor glucose ≤ 3.9 mmol/l were 31.0 (17–57) min and 26.0 (12–43) min, respectively ($P<0.0001$).

Thus, LGS was associated with 20% less time spent with glucose values ≤ 3.9 mmol/l and 20% less time with glucose values ≤ 3 mmol/l, compared with PLGM.

There were no significant differences between the three treatments in terms of time in glucose range 3.9–10 mmol/l (Table 2).

Similar results were found in a sensitivity analysis with weight proportional to the observed duration of use (data not shown).

Discussion

The results of this real-world study in 921 users in the UK show that use of low glucose suspend or predictive low glucose management was associated with low frequency and duration of hypoglycaemia in a real-world setting. Participants using low glucose suspend spent a median of 2.1% of time with glucose values ≤ 3.9 mmol/l, and 0.3% of time with glucose values ≤ 3.0 mmol/l, and those using predictive low glucose management spent 1.8% and 0.3% of time, respectively; this is considered to be safer in terms of severe hypoglycaemia outcomes such as seizures, which are often associated with more prolonged hypoglycaemia [17]. The finding that the potential benefits of pump therapy with insulin suspension technologies seen in clinical trials [2,11] are generalizable to the real-world setting is clearly of great clinical relevance.

To further explore the causal association between increasing sophistication of the suspension algorithms and glycaemic control, a prespecified sub-analysis of individuals switching from one therapy to another was conducted. This showed that the use of any suspend feature leads to clear reductions in monthly rates of hypoglycaemia events, without any clinically significant impact on time in range or mean HbA_{1c}, and that the MiniMed 640G system offers additional value in those moving from low glucose suspend to predictive low glucose management. Importantly, estimated HbA_{1c} varied between 50 mmol/mol (6.7%) and 58 mmol/mol (7.5%), showing that the participants

had reasonably well controlled diabetes. In participants switching from low glucose suspend to predictive low glucose management, the reduction in monthly rates of hypoglycaemia events appeared to be greater for events with glucose <3.9 mmol/l than for events with glucose <3.0 mmol/l, a finding consistent with that of Zhong *et al.* [18]. This was to be expected, as the predictive low glucose management algorithm suspends insulin infusion based on predicted hypoglycaemia, rather than when hypoglycaemia actually occurs. It is noteworthy that the use of this feature was associated with decreases in the time with sensor glucose ≤ 3 mmol/l or ≤ 3.9 mmol/l, and in the number of nocturnal hypoglycaemic episodes, because nocturnal hypoglycaemia is associated with an increased risk of seizures [17,19].

This analysis was requested by NICE as a follow-up after recommendation for the MiniMed Paradigm Veo system for the management of people with Type 1 diabetes and disabling hypoglycaemia despite optimal management with CSII where available [12]. In the UK, CGM is recommended in adults with recurrent severe hypoglycaemia, and in children with frequent severe, impaired awareness or inability to recognize or communicate about symptoms (generally those aged < 5 years). These are particularly important groups as they are not routinely included in clinical trials. We believe that the data demonstrate similar benefits in both adult and paediatric populations. As the present study was a database analysis, we do not have information about the clinical indications for CGM in the participants, and it is possible that a few would be self-funding sensors to improve their diabetes control. However, given the high sensor usage, it is likely that a significant proportion of the participants included in this analysis were funded through the UK National Health Service as per NICE criteria, and represent those at highest risk of hypoglycaemia. Single-centre analyses support these findings [20].

Severe hypoglycaemia is estimated to affect ~30% of people with Type 1 diabetes in the UK and can cause significant anxiety and disruption to everyday activities [21]. Reducing rates of severe hypoglycaemia in this population could result in substantial cost savings through reducing emergency department visits and paramedic call-outs, and may improve quality of life by decreasing anxiety

about nocturnal hypoglycaemia [22]. The ability of CGM with alarms to reduce the risk of hypoglycaemia, especially in high-risk groups, has been well documented in clinical trials [23–25]. To comply with the NICE requirement, a designated, anonymized, data-gathering and interpretation program based on inputs from CareLink data management software was created; this proved to be a meaningful tool with which to assess device performance and glycaemic outcomes on a large population, providing health assessment and provider bodies, such as NICE, with the information required for outcome-based evaluations of interventions.

In contrast to some previous studies [18,26], participants in the present study are likely to have been at high risk of hypoglycaemia, because in the UK CGM is only recommended by NICE for individuals with recurrent severe hypoglycaemia. Data from one case series suggest a mean severe hypoglycaemia rate of five episodes in the year prior to starting CGM [20].

The present findings in a UK population are consistent with those of previous analyses of CareLink data from Western Europe, Canada and Israel [14,18]. Zhong *et al.* [18] reported that use of the MiniMed 640G 'suspend before low' feature was associated with lower percentages of sensor glucose values ≤ 3.9 mmol/l or ≥ 13.3 mmol/l, compared with days on which the feature was not enabled; furthermore, sensor values recovered more rapidly, and were more stable, following automatically resumed pump suspension events than after manually resumed suspension events [18]. Similarly, Battelino *et al.* [13] showed that glycaemic control, as measured by mean blood glucose and blood glucose standard deviation, improved with increasing rates of sensor usage [13]. In the latter study, the incidence of hypoglycaemic episodes was reduced by 50% in participants with the highest rates of sensor use compared with those with the lowest rates. This is consistent with previous studies [27–29] which have shown that CGM should be used at least 70% of the time – considerably less than the usage seen in the present study – in order to achieve the maximum benefit.

Strengths of the present study include the large dataset and the real-world setting. Limitations include the lack of demographic data in the database, and the non-randomized nature of the study.

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Furthermore, we were only able to analyse data from users who had provided consent to the use of their anonymized data for research. Clearly, we cannot speculate on whether the characteristics of these individuals differ from those of individuals who did not provide consent, but we believe that the high rate of consent (~94%) renders the dataset representative of the entire CareLink population. In addition, the initial analysis was based on treatment groups of different sizes and durations of treatment, and no information is available regarding factors affecting the choice of device in an individual. Furthermore, the reasons for using SAP therapy without any suspension mode activated, and for switching to low glucose suspend, were not available; common causes of changes from low glucose suspend to predictive low glucose management might include on-going problematic hypoglycaemia despite low glucose suspend, or using low glucose suspend systems that had come to the end of their warranty and been replaced with the MiniMed 640G system. For the above reason, the analysis was purely descriptive, and no formal statistical comparison was possible. However, it was possible to perform inter-individual comparisons in participants who switched therapies for any reason, and we believe that these provide useful information about the potential benefits of the different technologies.

In conclusion, the present study showed that a low frequency and duration of hypoglycaemia can be achieved with insulin suspension technologies during routine use in individuals with Type 1 diabetes in the real-world setting. Individuals with problematic hypoglycaemia should be allowed access according to the NICE policy.

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Competing interests

P.C. has received consultancy and/or speaker fees from Medtronic, Dexcom, Roche, Novartis, Novo Nordisk, Lilly and Sanofi. S.P., A.A. and J.C. are employees of Medtronic, and S.P. holds Medtronic shares. F.M.C. has received speaker fees and support to attend advisory boards and clinical meetings from Novo Nordisk, Lilly Diabetes, Ypsomed, Dexcom, Medtronic and Abbott.

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Table 1 Glycaemic measures and use of glucose suspend features

	SAP			LGS			PLGM		
	Adults (n=58)	Children (n=45)	P	Adults (n=143)	Children (n=119)	P	Adults (n=316)	Children (n=465)	P
Total number of days using device	8503	5036		23 718	20 742		71,136	121,297	
Days using device	109 (38–168)	45 (30–139)	0.082	111 (46–245)	106 (41–298)	0.950	177 (66–350)	233 (84–389)	0.008
Time using CGM, %	95 (84–100)	97 (88–99)	0.468	97 (87–100)	96 (86–100)	0.741	99 (91–100)	99 (92–100)	1.000
Sensor glucose, mmol/l	8.2 (7.4–9)	8.5 (7.9–9.6)	0.117	9.1 (8.1–10.3)	9.1 (8.2–10.1)	0.897	9.3 (8.4–10.2)	9.6 (8.8–10.6)	0.000
	8.3 ± 1.3	8.8 ± 1.5		9.3 ± 1.7	9.2 ± 1.5		9.4 ± 1.5	9.7 ± 1.3	
Coefficient of variation of sensor glucose, %	36 (34–40)	39 (36–42)	0.015	35 (32–39)	39 (35–42)	<0.0001	35 (32–38)	38 (36–41)	<0.0001
Time in range 3.9–10 mmol/l	70 (64–80)	67 (58–75)	0.112	63 (52–74)	62 (52–73)	0.936	64 (54–73)	59 (51–67)	<0.0001
70–180 mg/dl), %									
Time ≤3.0 mmol/l (54 mg/dl), min	12 (4–30)	11 (5–22)	0.848	4 (1–10)	5 (2–10)	0.191	3 (1–7)	4 (2–7)	0.066
Time ≤3.9 mmol/l (70 mg/dl), min	58 (24–97)	57 (31–88)	0.740	27 (13–51)	34 (21–60)	0.018	23 (11–41)	28 (16–42)	0.012
Low glucose threshold, mmol/l				3.8 (3.4–4.2)	3.8 (3.3–4)	0.421	3.6 (3.4–4)	3.6 (3.4–3.8)	0.547
Automated suspends per day				0.7 (0.3–1.3)	1 (0.6–)	0.001	2.5 (1.7–3.2)	3 (2.3–3.7)	<0.0001
Duration of suspension per day, min				44 (25–55)	37 (27–45)	0.064	58 (50–65)	53 (47–58)	<0.0001

Estimated HbA _{1c} , mmol/mol	51 ± 8.8	55 ± 10.4	58 ± 11.6	57 ± 9.9	59 ± 10.6	61 ± 9.2
Estimated HbA _{1c} , %	6.8 ± 0.8	7.2 ± 1	7.5 ± 1.1	7.4 ± 0.9	7.5 ± 1	7.7 ± 0.8
		0.117			0.897	0.001

CGM, continuous glucose monitoring.
SAP, Sensor-augmented pump alone. LGS, Low glucose suspend. PLGM, predictive low glucose management
Data are presented as median (25th–75th percentile) or mean ± SD unless otherwise indicated.
n is number of occasions the therapy was used.

Table 2 Within-participant comparison of sensor-augmented pump therapy with no suspension feature, sensor-integrated pump therapy with low glucose suspend feature enabled, and sensor-integrated therapy with predictive low glucose management feature enabled for duration of device use, time within glucose thresholds, and number of hypoglycaemic excursions

	SAP vs LGS (n=31)			SAP vs PLGM (n=55)			LGS vs PLGM (n=139)		
	SAP	LGS	P	SAP	PLGM	P	LGS	PLGM	P
Duration of use, days	109 (45–153)	104 (50–193)	0.9543	49 (30–121)	239 (79–363)	<0.0001	77 (37–211)	214 (86–360)	<0.0001
Sensor glucose values, mmol/l	148 (138–162)	156 (140–171)	0.0336	146 (135–164)	155 (140–170)	0.0008	164 (148–182)	168 (155–189)	0.0005
Time in range 3.9–10 mmol/l, %	68 (59–76)	67 (56–76)	0.7161	70 (62–80)	70 (62–80)	0.6671	63 (53–73)	62 (52–72)	0.2068
Time ≤3.0 mmol/l, %	1 (0–1)	0 (0–1)	0.001	1 (0–2)	0 (0–1)	<0.0001	0 (0–1)	0 (0–1)	0.0091
Time ≤3.9 mmol/l, %	4 (3–5)	3 (2–4)	0.0028	4 (2–6)	2 (1–3)	<0.0001	2 (1–4)	2 (1–3)	<0.0001
Sensor hypoglycaemic event (<3.0 mmol/l)									
Duration, min	56 (41–76)	42 (30–58)	0.0106	59 (43–76)	47 (35–60)	0.0055	40 (25–54)	44 (33–56)	0.0445
Rate per month*	3.4	2.1	0.0091	3.8	2	<0.0001	1.6	1.3	0.0274
Daytime rate per month*	1.7	1	<0.0001	1.6	1	0.0019	0.8	0.7	0.1256
Nocturnal rate per month*	1.7	0.9	0.0367	2.4	1	0.0004	0.7	0.5	0.0614
Sensor hypoglycaemic event (<3.9 mmol/l)									
Duration, min	62 (49–74)	56 (41–60)	0.0151	63 (49–74)	47 (43–55)	<0.0001	49 (40–63)	47 (41–55)	0.0233
Rate per month*	19.3	15.6	0.0333	20	13.7	<0.0001	11.5	9	<0.0001
Daytime rate per month*	13	9.2	0.0107	12.8	9.5	0.0045	7.7	6.3	0.0072
Nocturnal rate per month*	6.6	6.6	0.9916	7.9	4.9	0.0122	3.9	3.1	0.0471
Estimated HbA _{1c}									
mmol/mol	51 (48–56)	54 (48–60)	0.0336	50 (46–57)	53 (48–59)	0.0008	57 (51–64)	58 (53–66)	0.0005
%	6.8 (6.5–7.3)	7.1 (6.5–7.6)		6.7 (6.3–7.3)	7.0 (6.5–7.5)		7.3 (6.8–8.0)	7.5 (7.0–8.2)	

Data are presented as median (25th–75th percentile).

SAP, Sensor-augmented pump alone. LGS, Low glucose suspend. PLGM, predictive low glucose management

* Event rates and *P* values derived from a negative binomial mixed model.